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TITLE: Detection of Shock Mucosal Oxygenation

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Contract was terminated prior to accomplishment of the tasks or development of the final deliverable (sensor system). This termination was without prejudice and was necessitated by funding shortfall due to DARPA reprogramming.

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Approved for public release; distribution unlimited

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**13. ABSTRACT** *(Maximum 200* Children's Hospital Medical Center (CHMC), in conjunction with Polychip, Inc., was contracted by DARPA to design, develop, and build a novel ultra-low weight telemetry unit for the detection of battlefield circulatory shock, as part of DARPA's Advanced Biomedical Technology Program. CHMC succeeded in 12 months in developing the world's smallest RF-powered telemetry and microprocessor unit and had confirmed the fundamental physiologic requirements for a novel sensor to detect battlefield hemorrhagic injury and circulatory shock. At the time DARPA terminated the contract for convenience, the electronic and physiologic development programs were ahead of schedule and on budget. CHMC estimates that its program would have completed the scope of work within 18 months, providing the DoD with the first telemetered sensor that would have saved lives on the battlefield by rapidly alerting combat personnel to the existence of seriously wounded soldiers.

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# INTRODUCTION

CHMC was selected by DARPA in August, 1994 to design a novel telemetered microsensor that could be safely ingested by military personnel and report the onset of circulatory shock. In September 1995, CHMC was contracted to begin research and development of the microsensor.

Polychip, Inc. served as a subcontractor to Children's Hospital Research Foundation on ARPA BAA 94-014, "Detection of Shock by Mucosal Oxygenation" from September 26, 1995 until the contract was terminated for convenience on January 17, 1996. The goal was to design, prototype and test a final pill and data capture system capable of sensing and reporting intraluminal intestinal oxygenation and acidosis. Had the contract run to completion, Polychip would have delivered the following to CHRF:

1) probes for sensing temperature, pH, pCO2, and pO2 (not funded here; instead, to be provided by a distinctly funded scope, a Phase II SBIR)
2) an integrated microminiaturized sensor probe "pill" platform incorporating these probes, a processor, and r.f. telemetry, and
3) a telemetric data reader and the host/controller system.

DARPA funded development of the pCO2 and pO2 probes outside of the BAA scope in a distinct contract to Polychip, "Sensor Probe Implementation," Phase II ARPA SBIR 94-093. The start date was slipped by the government for ten months (to February 23, 1997) so no overlap occurred between the subcontract this report describes and the parallel contract originally intended to coordinate with it. Sensor probe development therefore took place only to a first revision stage.

At contract termination, the pill platform and telemetry host/controller development were ahead of schedule. The functional capability of the pill platform and telemetry host/controller system were demonstrated at DARPA and CHRF in October of 1996. Discrete lab testing is ready to begin on the sensor probe, pill substrate platform and host/ controller systems. The Rev 1.0 chemical probes, the Rev 2.0 platform, and the Rev 3.0 host system can be tested separately for the following basic system requirements: magnetic induction power transfer, microprocessor-based platform management, temperature core and electrochemical probe analog-to-digital conversion, data capture, memory & transfer functions, and digital data telemetry through the reader system and host computer.

CHMC had built a world-class physiology testbed for the sensor. A porcine shock model, which mimicked the pathophysiology of hemorrhagic shock in the battlefield was developed. Studies of shocked animals revealed that tonometry provided an early warning system for circulatory shock and was reliable, with a low-latency. Major advances were made in the pharmacotherapy of hemorrhagic shock, utilizing this model. Termination of the DARPA contract resulted in disbanding of the laboratory and loss of personnel.

# BODY

## 1. Sensor Probe Development

Polychip is developing microminiaturized transducers (the probes) to convert temperature and the partial pressures of carbon dioxide, oxygen and hydrogen into electrical signals. That development effort is funded through a distinctly funding scope, and would have been provided here at no cost to this contract, had termination not occurred. Early stage work on the sensor probes was completed without support from this contract. The temperature sensor was available so was incorporated into the integrated circuit platform design here. Lower power dissipation and greater accuracy than traditional external or thermistor based designs were achieved by using an internal semiconductor integrated circuit (IC) macrocell: ±0.5oC accuracy. Core temperature cell design and software was modified for operating at 37oC center range.

## 2. Platform Development

Development and demonstration of the platform were ahead of schedule when the contract terminated: Two revisions of the pill platform were developed and a catheter platform would also have been developed. The Rev 1.0 platform is the size of a Nickel and was miniaturized to the Rev 2.0 "Tylenol capsule sized" module. Functional capability of the pill platform was demonstrated in October of 1996. The Rev 2.0 pill platforms completed engineering development, and preliminary testing procedures was ready to begin on equipment in various lab environments and for data formats in porcine temperature trials. Much of the activity in the final three months concentrated on improving the Rev 3 platform design for temperature and single channel probe (pCO2) measurement capabilities.

The pill platform provided local power, data processing and radioing for the sensor probes. A new programming and testing protocol was developed to achieve greater A/D linearity. Ten alpha stage devices were tested for assembly and programming. One hundred units were stocked to assemble and program for the Rev 2.0 probes; these were scrapped after termination to reduce close-out costs.

## 3. System Integration

Polychip was responsible for developing a complete system to process the data captured at the sensor probe level and provide in a readable format. System integration has three requirements: a) programming device to set up pills for experiments and use. b) a telemetry reader device to power up and read data from the pill and c) a host computer system to manage programming and data storage and usage. The system integration of the pills was completed to a level suitable for experiments to test the validity and performance of the data capture and telemetry technology. The system demonstrated the capability for data capture from internal temperature, digital data & power magnetic induction telemetry. Future revisions would have had all three capabilities in one hand held device.

Programming device: The initial goal was to develop a programming device to program pills individually for specific experiments. An industry-standard semiconductor wafer tester is currently used to program pills in batches. The programming device was adapted from the wafer tester into a hand held format for use in engineering development and manufacturing test and by non-technical personnel.

Telemetry: The magnetic telemetry communication was demonstrated in October, 1997. Further trials were planned with the Rev 2.0 platform to trouble-shoot telemetry in an ingested environment.

Reader Device & Host Computer System: The Rev. 3.0 lab bench magnetic telemetry reader and serial port PC host system engineering was completed at the beginning of 1997 and, after contract termination, was sold back to the vendor to reduce shutdown costs. The system could be used to test the procedures, equipment environments and data formats for porcine trials.

## 4. Porcine Testbed

Alpha prototypes developed by Polychip were to be tested using a porcine model of severe hemorrhagic shock. The model had been qualified in Q3, in terms of latency and response to various forms of pharmacologic and volume resuscitation. Post-hemorrhagic treatment with glibenclamide, a K ATP channel inhibitor, or S-isopropylisothiourea, a non-selective potent nitric oxide synthase inhibitor, resulted in rapid restoration of tonometric parameters (pCO2), in agreement with splanchnic macrovascular blood flow, serum lactate levels, mean arterial pressure, renal cortical ATP, and cardiac index. Thus, CHRF had confirmed that tonometric determinations were suitable for rapid detection and quantitation of shock and its resuscitation. This would have allowed medics to track the response to resuscitation in the field and titrate volume and pharmacologic interventions using real-time physiologic end-points. CHRF had also improved the shock model by placing ultrasonic transit-time flowmeters on the ascending aorta. Future studies were to have utilized cardiac index directly as a guide to the degree of exsanguination used to generate severe hemorrhagic shock.

CHRF was ready to test the alpha prototype from Polychip, Inc. in its in vivo model of hemorrhagic shock, specifically to evaluate response, latency, drift, and accuracy of the alpha pill and a catheter embodiment, intended for resuscitation by field medics. The laboratory team and expertise developed by CHRF for the evaluation of the prototype were disbanded following DARPA termination of the contract.

# CONCLUSIONS

Children's Hospital Medical Center, in conjunction with Polychip, Inc., had developed a novel ultra-low weight telemetry unit and had confirmed the basic physiologic requirements for a novel sensor to detect battlefield injury and shock. The program was moving ahead of schedule, on budget, towards the development of a telemetered sensor that would have saved lives on the battlefield by rapidly alerting combat personnel to the existence of seriously wounded soldiers. Termination of the program halted further technologic development of the telemetered microsensor and resulted in a disbanding of the physiology laboratory developed to complete the sensor development.